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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/738,423	KING ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *113-119* is/are pending in the application.

4a) Of the above claim(s) *118* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *113-117, 119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/24/07 has been entered.

Claims 100, 103, 106 108, 111, 112 have been canceled. Claims 113-119 are newly submitted.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 3/29/07 and 5/24/07 response would be addressed to the extent that they apply to current rejection.

Election/Restrictions

Applicant is reminded that the elected invention (including the elected species) for examination in this application is drawn to a method of using attenuated tumor-targeted bacteria, and species election drawn to the combination of *Salmonella* and cisplatin.

It is noted new independent claim 113 is drawn to use of a genus of attenuated tumor-targeted bacteria, which would be examined, in terms of applying prior art, to the extent that read on the elected species, i.e. *Salmonella bacteria.* Claim 118 is drawn to a non-elected species.

Claims 113-119 are pending, however, claim 118 is withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 113-117, 119 are under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 114 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 114 recites the limitation "the attenuated tumor-targeted *Salmonella*". There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 113, 115-117, 119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claims are drawn to a method of inhibiting tumor growth comprising administering to a subject having a solid tumor an effective amount of a chemotherapeutic compound cisplatin and an attenuated tumor-targeted bacteria. Given the broadest reasonable interpretation, the claims embrace a method of using a genus of bacteria that is tumor-targeted. With respected to the essential material needed for practice the claimed invention, "tumor-targeted bacteria", the specification states:

> 2.8. TUMOR-TARGETED BACTERIA
> Genetically engineered Salmonella have been demonstrated to be capable of tumor targeting, possess anti-tumor activity and are useful in delivering effector

genes such as the herpes simplex thymidine kinase (HSV TK) to solid tumors (Pawelek et al., WO 96/40238).

In subsequent working examples, all of the illustrated embodiments are drawn to attenuated *Salmonella*. The specification fails to disclose the claimed genus of invention by drawings showing a common structure that qualifies a bacterium as "tumor-targeted" for example; or by reducing to practice, for example, providing a list of tumor-targeted bacteria, or by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention.

An adequate written description for a family of tumor-targeted bacteria requires more than a mere statement that it is part of the invention; what is required is a description of the bacteria themselves. With respect to method claims, adequate description of the methods first requires an adequate description of the materials, i.e. a family of tumor-targeted bacteria, which provide the means for practicing the invention. The court has made it very clear "CONCEPTION OF CHEMICAL COMPOUND REQUIRES THAT INVENTOR BE ABLE TO DEFINE COMPOUND SO AS TO DISTINGUISH IT FROM OTHER MATERIALS, AND TO DESCRIBE HOW TO OBTAIN IT, RATHER THAN SIMPLY DEFINING IT SOLELY BY ITS PRINCIPAL BIOLOGICAL ACTIVITY". *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

The Revised Interim Guidelines state "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (Column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS",

"IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (Column 2, page 71436).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the numerous bacteria capable of tumor targeting. Therefore, only the described attenuated *Salmonella* meets the written description provision of 35 U.S.C. §112, first paragraph.

Claims 113, 115-117, 119 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting the growth of a solid tumor

cancer comprising administering to a subject in need an effective amount of one or more chemotherapeutic agents, supplemented with a msbB$^-$ *Salmonella* mutant (having genetically modified bacterial lipid A), does not reasonably provide enablement for inhibiting the growth of a solid tumor cancer supplemented with the genus of attenuated tumor-targeted bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

To the extent that the essential materials used in the claimed method are not adequately described by the instant disclosure, claims 113, 115-117, 119 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described, which is not conventional in the art.

The claims are drawn to using a genus of bacteria that are less toxic (attenuated) and capable of tumor targeting. The specification teaches genetically engineered [on

the lipid composition of] *Salmonella* have been demonstrated to be capable of tumor targeting, possess anti-tumor activity and are useful in delivering effector genes such as the herpes simplex thymidine kinase to solid tumors (Specification, § 2.8, paragraph 0040). Although the specification cites numerous prior art teaching that modification on lipid A pathway may reduce the ability of *E coli* bacteria to stimulate production of TNF-α (Specification, § 2.9), and thus reduce toxic effect to the host, the msbB$^-$ *Salmonella* mutant is the only bacterium taught in the specification to have tumor-targeting effect. The skilled artisan intending to practice the invention would have required to carry out undue experimentation to find out for themselves what the genus of "attenuated tumor-targeted" bacteria embraces. One cannot extrapolate the teachings of the specification to the scope of the claims because the skilled artisan cannot envision the detailed structures of bacteria encompassed by these claims, thus would not know how to use the invention without first carrying out undue experimentation to determine which non-*Salmonella* bacteria would have tumor targeting property.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention commensurate with the scope of the claims without undue experimentation.

Response to Argument

In the 3/29/07 response, the applicant indicated the new claims incorporate Examiner's suggestion regarding the msbB- mutant. In response, instantly rejected claims are still drawn to a method of using a genus of tumor-targeted bacteria.

In the 5/24/07 response, the applicant alleges,

> In the present case, Examiner makes a substantial assumption that is completely unsupported by any theory or evidence in the microbiological arts. Specifically Examiner assumes that the basis of the tumor-targeting phenotype can be reduced to a single, unitary "structure." There is no data on record or in the art to even suggest that this is the case. Therefore, basing the rejection on this unsound scientific "hypothesis" is improper and is insufficient to set forth a prima facie case of vague and indefinite claim language.

In response, it is the applicant who claims using a genus of tumor-targeted bacteria. Since there is no data on record or in the art knowing the genus exists, it is the applicant's duty to adequately describing how to identify the genus of bacteria. The Office did not assume any theory or structure for the genus of tumor targeted bacteria. The Office only requires the applicant provide an adequate descriptions for the genus, so that one skilled in the art would be able to identify such bacteria in order to practice the claimed invention without undue experimentation. It is noted that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991). 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In re Fisher, 166 USPQ 18, 24 (CCPA 1970).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 113, 114, 116, 117, 119 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Low et al* (Nat Biotech 1999;17:37-41, IDS), in view of *Schachter et al* (Cancer Biother Radiopharm 1998 Jun;13:155-64).

Low et al teach a method of treating tumor using a strain of *Salmonella* having disruption in msbB gene (msbB$^-$ mutant), said disruption reduces TNF-α induction (attenuated) and increases the LD_{50} of this pathogenic bacterium by 10,000-fold. The mutant *Salmonella* retains its tumor-targeting properties, i.e. exhibiting tumor accumulation ratios in excess of 1000:1 compared to its distribution in normal tissues. Administration of the msbB$^-$ *Salmonella* bacteria to melanoma-bearing mice results in reduced volume of solid tumors in the treated group compared to untreated controls (e.g. figs. 4, 5). *Low et al* conducted the test in mice, swine, human monocytes and mouse macrophages, and concluded that [the results] "HAVE BEEN CONSISTENT WITH THE NOTION THAT THE MSBB- BACTERIA CAN BE SAFE FOR USE IN HUMANS" (2nd paragraph, page 40). The teaching of *Low et al* differs from instant claims in that it does not explicitly teach

combining the bacteria therapeutic regimen with a chemotherapeutic agent such as cisplatin.

Schachter et al supplemented *Low et al* by disclosing a routine regimen of chemotherapy comprising cisplatin (a chemotherapeutic agent) for treating human melanoma, and establishing that it was well known in the art a combined drug therapy had been clinical routine since one single drug was insufficient for combating cancer. *Schachter et al* further supplemented *Low et al* by illustrating it was within the level of the skilled to combine a routine chemotherapeutic regimen with a newly developed biotherapy in treating solid tumors such as melanoma. *Schachter et al* presented a chemo-biotherapy protocol for patients with metastasis melanoma by including cytokines that regulate patients' immune system with conventional chemotherapy. The rationale for the design of the combined therapy was to achieve a higher percentage of a complete response (CR, meaning disappearance of all measurable disease) to drug treatment. *Schachter et al* teach that conventional chemotherapy such as a 4-drug regimen (BCNU, DTIC, **cisplatin** and tamoxifen) could have 40-50% response rate in patients being treated, but only 10-14% of patients achieved a complete response. When using the chemo-biotherapy, the response rate was 50%, and the complete response rate was up to 22%. *Schachter et al* do not specifically teach the tumor-targeted bacteria, but illustrated the need of further improvement of the conventional chemotherapy.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to seek newly developed therapeutic regimen in the art

and combine such with a routine drug regimen, and it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the attenuated tumor-targeted mutant *Salmonella* therapy as taught by *Low et al* with a routine chemotherapeutic regimen as taught by *Schachter et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention for maximal therapeutic effects. Given the state of the art that the conventional therapy alone was often insufficient in combating cancer, given the skilled was constantly searching for new means to improve cancer treatment, and given that each of the cited references teaches an agent that is effective in cancer therapy, one would have had a reasonable expectation of success when combining the two. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

In the remarks, applicant asserts, "use of tumor-targeted bacteria in a combination chemotherapy regimen goes against commonly accepted thinking in the chemotherapy arts" because chemotherapy could lead to a severely compromised ability of the cancer patient to fight infection against bacterial and fungal pathogens.

In response, as an initial matter, almost each of chemotherapeutic drug in cacner therapeutic regimen would weaken immune system individually, but the skilled artisan still combine them for the need of combating hard to kill tumor cells, it is a matter of balancing the beneficial and damaging effect of an anti-cancer drug. In the instant case,

Low et al clearly teach that the mutant strain of *Salmonella* was attenuated by auxotrophic mutations that would limit their pathogenesis in normal tissues but retained high-level replication within the tumors following systemic administration (see 1st paragraph, page 37). Apparently, *Low et al* was aware of the potential hazard of using the bacteria in cancer therapy, and attempting to minimize the toxic effect but utilizing its tumor-targeting effect. Further, as shown by *Schachter*, it was within the levels of the skilled to determine the right timing of the combination therapy. For example, *Schachter et al* did not use the biotherapy with the chemotherapy simultaneously, rather, they use such sequentially, i.e. modulating a patient immune system before or after the chemotherapy. Accordingly, it would have been within the knowledge of the skilled in the art to wisely use the newly developed bacteria therapy with a conventional chemotherapy sequentially to minimize side effects.

Applicants then argue that *Low* does not teach any combination therapy at all, and thus the prior art does not provide any motivation to combine. In response, the motivation was clearly suggested in the teaching of *Schachter et al.*

Applicants go on to argue that the Office has not provided a single piece of evidence that tumor-targeted bacteria are art-recognized equivalents of IFN-a and or GM-CSF. Applicants also argue that there is no suggestion to specifically combine the cisplatin with the tumor-targeted bacteria.

In response, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the

references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Here, the Office does not suggest that the attenuated bacteria is an equivalent of cytokines use by *Schachter et al*, rather, *Schachter et al* is relied on for a general desirability of combining a new therapeutic regimen with an existing conventional one. In a clinical setting, the skilled rarely uses only one drug/one type of therapy in a cancer therapeutic regimen, combining a chemotherapy with radiotherapy or newly developed cytokine, bacteria, gene therapy is often the routine.

Also, "FINDING OF MOTIVATION TO COMBINE PRIOR ART REFERENCES NEED NOT BE SUPPORTED BY SHOWING THAT CLAIMED COMBINATION IS PREFERRED OVER OTHER ALTERNATIVES, SINCE PROPER INQUIRY IS WHETHER THERE IS SOMETHING IN PRIOR ART AS WHOLE TO SUGGEST DESIRABILITY, AND THUS OBVIOUSNESS, OF MAKING COMBINATION, NOT WHETHER THERE IS SOMETHING IN PRIOR ART AS WHOLE TO SUGGEST THAT COMBINATION IS OR REFERRED OR MOST DESIRABLE". (*In re Fulton*, 73 USPQ2d 1141 CA FC 2004, emphasis added) Here, both *Low et al* and *Schachter et al* teach solving a problem in treating tumor and the need for new weapons in cancer therapy. Thus it would have suggested to the skilled artisan to look to references relating to possible solutions. It was within the levels of the skill to pair a existing known chemotherapeutic agent with the attenuated tumor-targeting bacteria with a reasonable expectation of success.

Applicants then argue that rational behind in re Kerkhoven is incorrectly applied because the technical subject in kerkhoven is far more predictable than that in the present case.

In response, the bacteria therapy has been proven effective in treating melanoma by *Low et al*, and the cisplatin has been proven effective in treating melanoma as shown by *Schachter et al*. It would have been *prima facie* obvious to one of ordinary skill in the art to combine these compositions to generate a new composition for the treatment of cancer with a reasonable expectation of success. Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See In re O'Farrell, 7 USPQ2d 1673 (CAFC 1988).

The applicant argues that they have shown a synergism between attenuated *Salmonella* and Cisplatin or cytoxan, which cannot be predicted by the combined teachings in view of the results of mitomycin C in figure 39.

In response, it is noted mitomycin C alone does not have much of a effect compared to the control, and thus, one would not expect this would change when combined with the *Salmonella*. As to the synergistic effect, it was achieved by a particular drug with a particular strain of *Salmonella*, thus the scope of the claims should limited to the bacteria strain. The court has determined, "WHETHER THE UNEXPECTED RESULTS ARE THE RESULT OF UNEXPECTEDLY IMPROVED RESULTS OR A PROPERTY NOT TAUGHT BY THE PRIOR ART, THE "OBJECTIVE EVIDENCE OF NONOBVIOUSNESS MUST BE COMMENSURATE IN SCOPE WITH THE CLAIMS WHICH THE EVIDENCE IS OFFERED TO SUPPORT." IN OTHER WORDS, THE SHOWING OF UNEXPECTED RESULTS MUST BE REVIEWED TO SEE IF THE RESULTS OCCUR OVER THE ENTIRE CLAIMED RANGE. *IN RE CLEMENS*, 622 F.2D 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)" ((MPEP 716.02(d), emphasis added)). Accordingly, until the claims are limited to

the scope of what it takes to get to the synergistic (unexpected) results, the rejection stands.

Accordingly, for reasons of record and set forth *supra*, the rejection stands.

Claim 115 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Low et al* (Nat Biotech 1999;17:37-41, IDS), in view of *Schachter et al* (Cancer Biother Radiopharm 1998 Jun;13:155-64) as applied to claims 113, 114, 116, 117, 119 above, further in view of *Pawelek et al* (Cancer Res 1997;57:4537-44, IDS).

Claim 115 is directed to specifically treating colon or lung cancer. *Low et al* in view of *Schachter et al* illustrated the tumor-suppressing effect of attenuated *Salmonella* in melanoma, not particularly lung or colon cancer.

Pawelek et al supplemented the teaching by establishing it was well known in the art that the attenuated *Salmonella* is capable of targeting multiple tumors including colon and lung carcinoma (e.g. paragraph bridging 4537-8, fig. 2).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method as taught by *Low et al* in view of *Schachter et al* for treating colon or lung cancer with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the lack of cure in cancer therapy in general, and the need for developing new therapeutic regimens for treating any type of cancer including colon and lung cancer. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service

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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
June 18, 2007